UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,601	06/10/2005	Reinald Repp	221801-1010	7727

24504 7590 10/18/2006

THOMAS, KAYDEN, HORSTEMEYER & RISLEY, LLP
100 GALLERIA PARKWAY, NW
STE 1750
ATLANTA, GA 30339-5948

EXAMINER	
STAPLES, MARK	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 10/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/500,601	REPP, REINALD	
	Examiner	Art Unit	
	Mark Staples	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1 is/are rejected.

7)☒ Claim(s) 1 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 06/30/2004 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

1. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Sequence Compliance

2. This application is objected to because it does not include the statement "the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing" and, where applicable, includes no new matter, as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b) or 1.825(d). Correction is required.

Specification

3. The Abstract is objected to for use of the legal phraseology "whereby" in the first and last sentences. Appropriate correction is required.

4. The Specification is objected to for lack of referencing SEQ ID NO. 1, as given in the CRF, within the specification. Appropriate correction is required.

5. The Specification is objected to for missing a page number on the first page of the specification and the first page of the claim set. Appropriate correction is required. For later discussion, the first page of the claim set is given page number 12.

6. The specification is objected to because of the following informality: it lacks a heading "Brief Description of the Drawings" followed by a brief description pf the drawings under this heading. Correction is required. The in depth explanation of the drawings, as is now appropriately contained in the Specification, should remain in the body of the Specification.

Claim Objections

7. Claim 1 is objected to because of the following informalities: unclear grammar in the phrase "from binding to the primer-specific target sequence" found in claim 1 iii). The following or similar may be intended: "from binding of the solid-phase bound primer to the primer-specific target sequence". Appropriate correction is required.

8. Claim 1 objected to because of the following informalities: incorrect grammar in the phrase "as primer binding site" found line 2 of page 13. The following or similar may be intended: "a primer binding site". Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 1, the phrase "e.g." which is "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Regarding claim 1, the phrase "any other methods" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). It is unclear what methods may constitute "any other methods".

Regarding claim 1, the construction " at least one of the primers . . . comprises . . . the following elements . . . reamplification in a subsequent conventional PCR (nested PCR)" is indefinite since it is unclear as to what is intended by this language. It is unclear how reamplification, which is an active process step, can be an element of a primer, which is a product.

Regarding claim 1, the phrase "reamplification in a subsequent conventional PCR (nested PCR)" is further indefinite since it is unclear as to whether "nested PCR" is the only subsequent conventional PCR intended or whether "nested PCR" is intended as one of the subsequent conventional PCR that can be used.

Regarding claim 1, the phrase "characterized in that" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). It may be intended that the method has a

step comprising *providing* a pair of primers wherein one of the pair of primers comprises the elements given in step 1 a). If this or similar is intended, it is suggested for clarity, that this step be placed where it would occur sequentially in the method. It may be intended that such a step occur directly before or directly after step 1 i).

Claim 1 recites the limitation "the primer-specific target sequence" in lines 18 and 19 on page 12. There is insufficient antecedent basis for this limitation in the claim.

Claim 1 recites the limitations "*de-novo-synthesized* DNA molecules" in line 10, "*de novo* synthesis" in line 13, and "PCR" in line 13, all on page 13. There is insufficient antecedent basis for these limitations in the claim. The claim recites nucleic acids in line 10 on page 12 which includes RNA, and the terms "*de novo*" and "PCR" have no antecedent basis.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: 1 ii) how the amplification reaction is done; 1 iii) how the solid phase bound primers are added or introduced, and 1v) how the amplification products of step 1 ii) have acquired a fluorescent or radioactive label.

Claim 1 is also indefinite since the detection of step 1 v) is done on the amplification products of step 1 ii). How intervening steps 1 iii) and 1 iv) relate to the detection is unclear, as these steps do not appear to be involved in the method of

detecting nucleic acids. It may be intended that the reaction products released into the aqueous phase in step 1 iv) are detected.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the conformation change resulting in a double-stranded restriction site with a hairpin structure (see Specification page 7 lines 16 through 38 and Figures 1 and 2), does not reasonably provide enablement for any conformation change. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

A conformation change is broadly claimed which includes even the fundamental conformation change of primers annealing to target sequences to form a double-stranded helix. However, the nature of the invention is a method which uses the specifically disclosed conformation change to a double-stranded restriction site which is a hairpin structure. Without undue experimentation, one of ordinary skill in the art would not know how to use the method with other conformation changes. The inventor does not provide direction for use of other conformation changes. The only working example described in the specification and illustrated by Figures 1 and 2 is the one conformation change to a double-stranded restriction site which is a hairpin structure. The state of

the art is such that just having a conformation change by itself does not predict that the method can be used successfully to detect nucleic acids. The conformation change must have a certain structure in order for the method to be used.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claim1 is rejected under 35 U.S.C. 102(b) as being anticipated by Shapero et al. (Oct. 2001).

Regarding claim 1, Shapero et al. teach a method for detecting nucleic acids using solid-phase-bound primers comprising the steps

i) providing nucleic acids to be amplified (see Abstract for human genomic DNA),

ii) carrying out the amplification reaction using at least two primers, of which at least one is coupled with a solid phase (see Figure 2 and Table 1),

iii) generation of a cleavage site within the solid-phase-bound primers by a conformation change resulting from binding to the primer-specific target sequence (a

double stranded DNA is formed which is a conformation change from the single strand, see Figure 2),

iv) releasing the reaction products into the aqueous phase by cleavage within the cleavage site generated in ii) by conformation change, e.g. with the aid of a restriction enzyme (a restriction enzyme cleaves/digests the double stranded conformation change at the restriction site see Figure 2),

v) detecting of the amplification products formed via optical and chromatographic methods (see Figure 1),

wherein

a) at least one of the primers employed for the amplification reaction comprises, in 5'-3' direction, the following elements: coupling site for the solid phase (see Figure 2), a first target-sequence-specific segment (see Figure 2), a cleavage site generable by conformation change (see Figure 2), reamplification in a subsequent conventional PCR reaction (see Figure 1 and 1st paragraph of Results section on p. 1927 for subsequent second and third amplification cycles), a primer binding site for a sequence reaction or for further functions, and a second sequence which is specific for the nucleic acid to be amplified (see Figure 2),

b) de-novo-synthesized DNA molecules are transferred into the aqueous phase by cleavage with a restriction enzyme either still during the de-novo synthesis or after the PCR amplification cycles (entire reference, especially Figure 1 A and Figure 2).

12. Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 6,949,633 (filed 1998).

Regarding claim 1, US Patent No. 6,949,633 teaches a method for detecting nucleic acids using solid-phase-bound primers comprising the steps

i) providing nucleic acids to be amplified (see Figure 16 and description of Figure 16 found),

ii) carrying out the amplification reaction using at least two primers, of which at least one is coupled with a solid phase (see Figure 16 and description of Figure 16 found in column 17 lines 7-12 and column 23 lines 6-28),

iii) generation of a cleavage site within the solid-phase-bound primers by a conformation change resulting from binding to the primer-specific target sequence (see Figure 16 and description of Figure 16 found in column 17 lines 7-12 and column 23 lines 6-28),

iv) releasing the reaction products into the aqueous phase by cleavage within the cleavage site generated in ii) by conformation change, e.g. with the aid of a restriction enzyme (see Figure 16 with description of Figure 16 found in column 17 lines 7-12 and column 23 lines 6-28 including a hairpin structure; and section 4.3.2 Cleavage beginning in column 41 line 11),

v) detecting of the amplification products through radioisotopes and fluorophores (see column 41, lines 47-51),

wherein

a) at least one of the primers employed for the amplification reaction comprises, in 5'-3' direction, the following elements: coupling site for the solid phase, a first target-sequence-specific segment, a cleavage site generable by conformation change, reamplification in a subsequent conventional PCR reaction (including nested PCR, see column 14 line 29), a primer binding site for a sequence reaction or for further functions, and a second sequence which is specific for the nucleic acid to be amplified (see Figure 16 and description of Figure 16 found in column 17 lines 7-12 and column 23 lines 6-28),

b) de-novo-synthesized DNA molecules are transferred into the aqueous phase by cleavage with a restriction enzyme either still during the de-novo synthesis or after the PCR amplification cycles (entire reference, especially Figure 16 and description of Figure 16 found in column 17 lines 7-12 and column 23 lines 6-28).

References of Record

13. Adessi et al. (2000) is made a matter of record as a reference of interest regarding the instant application. Adessi et al. teach many of the elements of the claimed invention. Adessi et al. teach cleavage of the bound amplification products, but do not specifically teach that this is due to a conformational change in the bound products (see p. 7, 2nd column, 4th sentence).

Mayer et al. (1996) is also made a matter of record as a reference of interest regarding the instant application. This reference teaches the use of nested PCR after standard PCR.

Conclusion

14. No claim is free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples
Examiner MS
Art Unit 1637
October 13, 2006

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
10/16/06